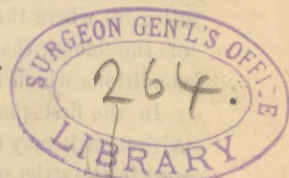


Pepper (Wm)

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ART. I.—*Progressive Pernicious Anæmia, or Anæmatosis.* By WILLIAM PEPPER, M.D., Physician to the Philadelphia and to the Children's Hospital; Prof. of Clinical Medicine in the University of Pennsylvania, etc.

THE following cases are offered as a contribution to the study of one of the most obscure and ill-understood classes of disease. The improvements in our knowledge of diagnosis, aided by the introduction of the use of organic chemistry and of the microscope into the study of the physical characters of the blood, have led to much attention being devoted of late years to those remarkable affections which present as one of their chief characteristics a profound change in the composition of this fluid. The result has been the gradual establishment of several hitherto unrecognized diseases, and the much more exact description of other already familiar conditions. But, in spite of this decided advance in our knowledge of the symptoms and lesions of these affections, it cannot be claimed that much progress has yet been made in our acquaintance with their true intimate nature or mutual relations. The group of diseases to which I refer may be said to include—without any pretension to fix positively its limits—anæmia in some of its rarer forms; leukæmia; pseudo-leukæmia, adenia, lymph-adenoma, or Hodgkin's disease; and Addison's disease.

They are usually classified under some such heading as General or Constitutional Diseases, because the entire system is evidently affected. But they are clearly distinguished from other general diseases, such as the great class of fevers, by the fact that they are not dependent, so far as known, upon the introduction of any specific morbid principle into the economy; but are due to an essential and progressive alteration of the blood, usually if not always associated with or dependent upon some lesion of the solids.

In view of the progressive mal-nutrition which marks these affections, the term *Cachexia* (constitutional dystrophy of Jaccoud) is correctly used to describe them. There are other features which may be mentioned as distinguishing these Cachexias. For the most part they arise without definite recognizable cause; they are not self-limited, and have no definite duration; their tendency is to an unfavourable termination, and indeed in regard to most of them it may be said that they are invariably fatal.

In placing anæmia in this list of Cachexias, it must be noted that I have limited myself to certain comparatively rare forms only of that condition. Indeed the name anæmia has been so long used in a vague way to cover all cases where there are pallor of the surface and the evidences of poverty of the blood, that it is necessary to define with some care the different conditions which have thus been included.

In the first place there is the true anæmia which follows hemorrhage. Although it may be objected that there can never be *anæmia* or *bloodlessness* in the strict sense of the term, and that consequently the term *hypæmia* should be used, the important fact is that there is a simple reduction in the mass or amount of the blood without morbid change in its elements, and custom has so sanctioned the use of the term "anæmia" that it seems undesirable to discard it.

Secondly, we frequently observe that, when there has been severe loss of blood, or after prolonged suppuration or continued morbid discharges of any kind, there is a diminution in the red globules, and also a reduction in the proportion of albuminous and saline elements, while the bulk of blood remains normal in consequence of an excess in the proportion of water. To this condition the term *hydræmia* appears most applicable.

But, thirdly, there are also cases met with where, although the mass of the blood may be diminished, the chief change is a progressive and often seemingly causeless diminution in the proportion of the red globules. It is evident in such cases that a profound alteration in the blood-making function is present; and it is most probable that the chemical composition and vital properties of the red globules are also affected, and that there is, at the same time, some alteration in the properties of the white corpuscles, though their number or appearance be not materially changed. Still the diminished proportion of red globules is the most striking feature; and as "anæmia" is a particularly bad name for such a condition, attempts have been made to coin some special term to distinguish it. Thus it has been called *oligocythæmia* (ὀλιγος, few; κύτος, cell; αἷμα, blood), *aglobulia* and *hypoglobulia*. All of these, however, seem open to objection, and have failed to establish themselves in common usage. Jaccoud (Path. Interne, tome ii. p. 820) clearly distinguishes this *essential globular anæmia*, but is, it appears to me, less acute and logical than usual in applying the term chlorosis to it. This name has been for so long a time specially devoted to an affection which presents anæmia among its symp-

toms, it is true, but which has so many distinct peculiarities, and is, on the other hand, wanting in so many of the features of the grave forms of anæmia we are now referring to, that it seems erroneous and confusing to endeavour to include them both under this title. I would therefore much prefer restricting the term "chlorosis" to the disease with which it has long been familiarly connected.

If we were to look merely to the chief physical alteration in the blood, I should be disposed to suggest the name of *anerythræmia* (from *a*, *privative*; *ερυθρος*, *red*; *αἷμα*, *blood*); but it is desirable that the term finally adopted should express not merely this one anatomical condition, but should refer to the pathological nature of the affection. I will postpone, therefore, the suggestion of a name which I trust may meet with approval, until the attempt has been made to determine the pathological nature of the form of anæmia under discussion. (See p. 342.)

In a few cases we are able to clearly explain the production of this globular anæmia. We know, for instance, that some mineral poisons, such as phosphorus, the mineral acids, etc., produce intense anæmia when their toxic effects are thoroughly induced; and that it is probably due to a direct action of the poison upon the globules. But when we leave such cases, we find that an explanation of the various forms of essential globular anæmia demands that we should be acquainted with the manner in which and the place where the red globules are developed: and until this vexed physiological question is definitely settled, it is simply impossible to determine finally the intimate nature and mutual relations of these interesting forms of disease.

For some time the generally accepted view has been that the lymphatic glands and spleen are specially concerned in the maintenance of the normal composition of the blood. It appears that from the lymphatic glands, and probably also from the lymphoid Malpighian corpuscles in the spleen, the white corpuscles are developed and enter the blood. It seems probable that some, at least, of the red globules result from the gradual transformation of the substance of the white cells. Less is known as to the mode and place of death of the red globules, though there is reason to believe that the splenic pulp is specially concerned in this process, while recent observations tend to connect the liver also with it.

But quite recently the brilliant observations of Neumann¹ and Bizzozero² have demonstrated the resemblance between some of the cellular elements of the marrow of bones and of the splenic pulp, and have rendered it probable that the former also is connected with the processes of transformation which the blood globules undergo either in formation or destruction. I will now merely state that this discovery has been so fully confirmed by both physio-

¹ Centralb. f. d. Med. Wiss. 1868, p. 689; Arch. d. Heilk. Bd. x. pp. 68 u. 220.

² Gazzetta Medica Lombarda, 1868, No. 46; 1869, No. 2.

logical and pathological observations, that it may be stated that the marrow of the bones is to be added to the spleen and lymphatic glands as being intimately concerned with the maintenance of the normal morphological constitution of the blood.

Beyond this point physiology has not yet advanced, and one of the most interesting and important fields for pathological research lies in the direction of these cachexias and in attempting to trace their intimate causes, nature, and mutual relations.

My present purpose is to offer a contribution to this important study by calling attention to a peculiar form of anæmia of obscure and fatal character, which has recently been redescribed, as though it were a new affection, under the name of "Progressive Pernicious Anæmia." I doubt not that many who read this article will recall cases in their own experience where, without apparent cause, extreme anæmia developed itself and gradually progressed, in spite of all treatment, to a fatal issue, and where the absence of any gross lesion which was so puzzling during life was corroborated at the autopsy. Many, too, who are familiar with the clinical writings of the last thirty or forty years may recall descriptions of just such cases, recorded under various names, *idiopathic*, *malignant*, or *essential anæmia*, *grave form of chlorosis*, etc., and with a candid avowal of the utter obscurity of their true nature. As the present article has no pretension of being a complete historical memoir upon this form of anæmia, I will limit myself to alluding to the cases of fatal chlorosis by Marshall Hall (Am. ed. *Practice of Medicine*, 1839, p. 367), and especially to the cases of "idiopathic anæmia," to which Addison (Syd. Soc. ed. of his works, 1868, p. 212) refers in the following language:—

"It makes its approach in so slow and insidious a manner that the patient can hardly fix a date to his earliest feeling of that languor which is shortly to become so extreme. The countenance gets pale, the whites of the eyes become pearly, the general frame flabby rather than wasted; the pulse, perhaps, large, but remarkably soft and compressible, and occasionally with a slight jerk, especially under the slightest excitement; there is an increasing indisposition to exertion, with an uncomfortable feeling of faintness or breathlessness on attempting it; the heart is readily made to palpitate; the whole surface of the body presents a blanched, smooth, and waxy appearance; the lips, gums, and tongue seem bloodless; the flabbiness of the solids increases; the appetite fails; extreme languor and faintness supervene, breathlessness and palpitations being produced by the most trifling exertion or emotion; some slight œdema is probably perceived about the ankles; the debility becomes extreme. The patient can no longer rise from his bed, the mind occasionally wanders, he falls into a prostrate and half-torpid state, and at length expires. Nevertheless, to the very last, and after a sickness of perhaps several months' duration, the bulkiness of the general frame and the obesity often present a most striking contrast to the failure and exhaustion observable in every other respect. With perhaps a single exception, the disease, in my own experience, resisted all remedial efforts, and sooner or later terminated fatally. On examining the bodies of such patients after death, I have failed to discover any organic lesion that could properly or reasonably be assigned as an adequate cause of such serious consequences; nevertheless, from the disease having uniformly occurred in fat people, I was naturally led to entertain a suspicion

that some form of fatty degeneration might have a share, at least, in its production; and I may observe that, in the case last examined, the heart had undergone such a change, and that a portion of the semilunar ganglia and solar plexus, on being subjected to microscopic examination, was pronounced by Mr. Quekett to have passed into a corresponding condition."

This admirable passage is extracted from Dr. Addison's classical memoir "*On the Constitutional and Local Effects of Disease of the Supra-renal Capsules*," published in 1855; and it gains interest from the fact that it was while studying these cases of idiopathic anæmia that he observed the equally curious cases of anæmia with bronzing of the skin, which he showed to be connected with disease of the supra-renal capsules, and which are now known the world over by his name. It also shows very clearly that this form of anæmia was well recognized, was occasionally encountered, and was made the subject of public clinical discussion before 1850 (although not published until 1855). Unfortunately no microscopic examination of the blood was made.

About this time, however (1845 to 1850), Virchow and Bennett called attention to leucocythæmia or leukæmia, and since then, until very recently, nearly all cases of progressive fatal anæmia have been in some way connected with that interesting disease. It will be remembered that leukæmia is characterized by an extreme increase in the number of white corpuscles in the blood, together with a marked reduction in the number of red globules and the mass of the blood, and that three varieties, *splenic*, *lymphatic*, and *medullary* or *myelogenic*, have been described, according as the chief seat of the lesions is found in the spleen, the lymphatic glands, or the marrow of the bones respectively.

Subsequently it has been found that there exists a form of cachectic anæmia with diffused enlargement of the lymphatic glands (such as occurs in lymphatic leukæmia), which was first described by Dr. Hodgkin (*Medico-Chirurgical Transactions*, vol. xvii. p. 68, 1832), and which may pass through all its stages to a fatal issue without any increase in the proportion of white corpuscles in the blood. This variety of anæmia has been described by several writers under the names of Hodgkin's disease (Wilks); Lymphatic Anæmia; Adenia (Trousseau); Pseudoleukæmia (Cohnheim and Wunderlich). Still further, it has been found that in some rare instances this progressive anæmia, without leukæmic complication, may be connected with enlargement of the spleen instead of the lymphatic glands, thus constituting a *splenic anæmia* (Griesinger), *splenal cachexia* (Wood), or *splenic form* of pseudoleukæmia.

Finally, it has been shown by Ponfick¹ and Wood² that in some cases of pseudoleukæmia there may be not only lesions of the lymphatic glands

¹ Ü. d. Sympathischen Erkrankungen des Knochenmarkes bei inneren Krankheiten. Virchow's Archiv. 56, Bd.

² On the relations of Leucocythæmia and Pseudoleukæmia, Amer. Journ. Med. Sciences, Oct. 1871, p. 373.

and of the spleen, but also an affection of the marrow of the bones similar to that which is found in some cases of leukæmia. It appears thus that there exist corresponding series of forms of these two affections, as follows :—

Splenic	} Leukæmia.	Splenic	} Pseudoleukæmia.
Lymphatic		Lymphatic	
Medullary		Medullary	

It is of course understood that, in many cases, lesions of two or even all three of these tissues are associated.

Now it will be found, I believe, that the symptoms of these cases of so-called pseudoleukæmia differ from those of "idiopathic anæmia" as described by Addison, or from the symptoms of the cases I will relate, only in the fact that enlargement of the spleen or lymphatic glands exists in the former.

It becomes then extremely important to study carefully this singular form of anæmia, the more so as there is reason to believe that its nature has been overlooked from Addison's time down to within a few years. I have myself met with three cases which are undoubtedly of this nature. And quite recently, moreover, a series of articles has been published containing the careful descriptions of cases of intense and fatal anæmia with fatty degeneration of the heart and other organs, which it is easy to see are identical with the affection described by Addison. Among the references which I have to such recent articles, the first in order of publication is the following case of "oligæmia," by Dr. Luigi Corraza,¹ of Bologna, in 1869.

A young woman, 24 years of age, had never entirely regained her health since an attack of continued fever at the age of 15 years. Subsequently she bore four children in five years, and about the middle of her last pregnancy had a severe attack of jaundice, which soon passed away, but left the skin of a dirty-yellowish colour. She was confined in November, 1867, but remained feeble, suffering frequently with diarrhœa, and when admitted to the hospital in January, 1868, presented the following symptoms: No emaciation, surface straw-yellow; marked dyspnœa and restlessness, headache, giddiness on rising, palpitation of heart, sense of weight and distress in stomach; anæmia. The temperature was normal; pulse and breathing accelerated: anæmic murmurs in the large vessels; the liver somewhat enlarged; the spleen and lymphatic glands not affected, and the extremities œdematous. These symptoms became aggravated, with vomiting, increased depression of circulation, and dyspnœa and somnolence, and death ensued on January 27th. At the autopsy there was œdema of the lungs, and some serous effusion in the pericardium and pleural and peritoneal cavities. The blood was very liquid. The heart, liver, and kidneys were fatty. The spleen was slightly swollen.

In the paper of Dr. Wood last referred to, which presents one of the most thoughtful and original contributions to the study of this obscure

¹ Storia di un caso di oligæmia con riflessioni su quest' affezione, sulla clorosi e sulla degenerazione grassosa degli organi, Bologna, 1869. Quoted at length in Meissner on Leukæmia and Pseudoleukæmia, Schmidt's Jahrb., 1872, Bd. 155, s. 333.

class of affections, there is one case at least which corresponds to the essential anæmia we are now considering.

Shortly afterwards, Gusserow¹ published a valuable article containing the careful clinical histories of five fatal cases of intense progressive anæmia, all occurring in pregnant women. In these cases no jaundice was observed, while, on the other hand, albuminuria was detected in one case, and there was some febrile elevation of temperature in several instances; but, with these exceptions, the patients presented the same train of symptoms, without any recognizable organic lesion, which has just been quoted from Corrazza's case. Careful post-mortem examination was made in every instance, and revealed the same conditions of fatty degeneration of the heart and sometimes of the liver and kidneys, with œdema of the lower lobes of the lungs and small amounts of reddish serous effusion into the various cavities. The blood was diminished in quantity; there was no increase in the proportion of white corpuscles, but great diminution in the red globules. The spleen was slightly enlarged, but with no characteristic change in its pulp; the lymphatic glands were not affected.

In the following year, 1872, Biermer, of Zurich,² published a very able memoir, based upon the study of fifteen cases of fatal anæmia which he had met with in five years. The majority of his cases occurred in women, and, as in Gusserow's cases, child-bearing seemed to predispose to the disease. He also noticed that in some instances the cause appeared to be chronic follicular catarrh of the intestines. He added to the clinical history of the disease that, late in its course, ecchymoses occasionally appear in the retina or under the skin, and sometimes hemorrhages may occur from the nose or kidneys. But in every essential particular—the gradually and inevitably fatal progress, absence of emaciation, extreme diminution of red globules without increase in number of white corpuscles, absence of lesions of spleen or lymphatic glands, presence of intense anæmic murmurs, passive dropsy, and other signs of alteration of the blood and failure of heart-power, and finally, in the detection of fatty degeneration of the heart and of various organs, as the only organic lesion of the solids after death—in every particular the cases of Biermer agree with those above quoted. With the idea that the affection was a new one, Biermer applied the name "Progressive Pernicious Anæmia" to it. But when the close resemblance between these recent reports and the older but equally clear description by Addison of "idiopathic anæmia" is carefully considered, the conclusion seems to me unavoidable that they are one and the same affection. It is not a little melancholy, if this conclusion be correct, to find that, in the native land

¹ Ü. hochgradigste Anämie Schwangerer, Arch. f. Gynækologie, 1871; Hft. 2, p. 218.

² Correspondenzblatt für Schweizerische Aerzte, Jahrgang 2, 1872, No. 1.

of that great clinical master, one of the leading journals¹ accepts "progressive pernicious anæmia" as a disease *sui generis*, and observes that no case has as yet been reported in Great Britain.

Still more recently, Immermann,² of Basle, has published two cases of identical character; and Zenker³ furnishes one more with complete and minute post-mortem examination.⁴ In an article published recently (*Boston Med. and Surg. Journ.*, Jan. 14, 1875, p. 33), Dr. James R. Chadwick, of Boston, reports a case of fatal anæmia, apparently due to repeated hemorrhages following delivery, the symptoms and course of which, as well as the results of post-mortem examination, show it to have been identical in nature with the cases hereafter reported. In the *Practitioner* for January of the present year (p. 22), Dr. Broadbent, in a paper on the "Therapeutic Uses of Phosphorus," describes two similar cases, one of which was studied until its fatal termination, and the diagnosis verified by the absence of any organic disease to explain the anæmia. In neither this case nor the one reported by Dr. Chadwick was the marrow of the bones examined. I should also add that in a remarkable memoir, Ponfick⁵ has described, from a purely anatomical point of view, at least one or two cases of this form of anæmia, under the name of "The Anæmic Form of Fatty Degeneration of the Heart."

Having now given a hasty sketch of this peculiar affection, and a sufficient number of references to recorded cases to show its comparative frequency, I propose to present the histories of three cases which have recently come under my observation, and then to consider more in detail its symptoms and pathology.

CASE I. *Intense anæmia (of malarial origin?); irregular fever, uncontrolled by quinia; œdema, gastric disturbance, palpitation, hæmic murmurs, hemorrhages, somnolence, coma, and death; no enlargement of spleen or lymphatic glands. No autopsy.*—The following history is chiefly based upon notes kindly furnished me by my friend Dr. R. G. Curtin, under whose care the case was, and with whom I visited the patient in consultation.

Eliza Farrell, aged twenty-six years, single, a dressmaker by occupation, and a tall, stout, hardworking woman, with a good family history. She lived on the outskirts of Philadelphia, in a somewhat malarious neighbourhood. Her father, who lived in the same house, had malarial neuralgia in 1872. In October, 1872, she applied at the Hospital of the University of Pennsylvania with a severe attack of bronchial catarrh, with some loss of flesh; there had been no hæmoptysis, the expectoration being copious, white, and frothy. There were very marked bronchitic râles over both lungs. The attack proved obstinate, but in the course of five months she seemed to have regained her health.

In September, 1873, she came again, complaining of great weakness, which had been increasing for some time. She had also anorexia and irregular fever

¹ Medical Times and Gazette, Nov. 21, 1874, p. 582.

² Deutsches Archiv. f. Klin. Med., 13ten Bd., 3tes Hft., 1874, s. 209.

³ According to the Medical Times and Gazette, a similar case, without autopsy, has been published by Gfrörer of Heilbronn, but I have not been able to discover the original record.

⁴ Id. Op., p. 348.

⁵ Ueber Fettherz, Berlin Klin. Wochenschrift, 1873, No. 192.

in the afternoons, and was decidedly anæmic. She was ordered arsenic, iron, and quinia.

A week later, September 27, she returned, stating that she felt much weaker, and that she now had slight chills in the afternoon, followed by more fever. Her feet and face were puffy, and there was a soft systolic cardiac murmur. The urine was free from albumen. The quinia was increased to sixteen grains daily.

October 11, she seemed better, and was free from fever. Her appetite was better and her feet less swollen, but she was still as weak and anæmic as before. She was ordered liq. ferri acetatis.

After this she grew steadily worse again, and was soon obliged to keep to her bed. She had several hemorrhages from the gums, and when she menstruated the flow was excessive. Her appetite and power of taking food diminished, and the œdema increased decidedly.

On November 4, her condition was as follows: The skin and mucous membranes seemed literally bloodless; the face and feet were very œdematous; the urine was free from the least trace of albumen; she had recently had a hemorrhage from the gums; she could take but very little food without inducing vomiting; the tongue was covered with a white, pasty fur; the bowels had been quiet throughout, though easily moved; there was *no enlargement* of the *spleen*; the mind was clear but sluggish, and there was extreme prostration; there was still irregular febrile action in the latter part of the day, disappearing and reappearing at irregular intervals.

November 14, she was first seen by me in consultation with Dr. R. G. Curtin. She had been steadily growing worse, and was now confined to bed, and any exertion caused faintness, and occasionally nausea and vomiting were caused merely by rising in bed. If possible, she was even more anæmic than before, and the bloodless condition of the cutaneous and mucous surfaces was truly remarkable. There was but little emaciation. There had been more hemorrhages from the gums. She vomited frequently, and could take but little nourishment; œdema of feet and face marked; no enlargement of spleen or lymphatic glands, or evidence of organic disease of any organ; no albuminuria; there were no petechiæ or ecchymoses; the action of the heart was rapid and very feeble; the pulse small and gaseous. There was a very loud anæmic murmur over heart, and remarkably strong venous hum was heard over the large veins, as the jugulars and subclavians. There was also a continuous, quite distinct, humming roar audible over the whole skull during arrest of breathing as well as during respiration; this was especially strong over the longitudinal and lateral sinuses. The patient was conscious of this and described it, saying that the constant roaring was very unpleasant.

The mind was clear, but could be fixed only for a short time on any subject. The patient lay for the most part in a heavy sleep. Microscopic examination showed absence of any increase in white corpuscles, but great diminution in the red globules.

November 28. Increasing weakness and hebetude of mind; condition otherwise much the same; no albuminuria or enlargement of spleen. Has continued to take large doses of quinia and iron, and utmost care has been used to administer nourishment both by the mouth and rectum.

December 4, there was a sudden increase in the swelling of the body, followed by coma, which persisted until her death occurred the following day.

Unfortunately no *post-mortem* examination was permitted, but still it is difficult to doubt the nature of the affection. Although the place of her residence was somewhat malarious, and it may be that malaria may have originally had somewhat to do with breaking down her nutrition, the course of the case, the utter inefficiency of quinia, iron, and arsenic, and the absence of enlargement of the spleen, made it clear that at least the later period of her illness was not merely malarious in character.

CASE II. Vague symptoms of failing health; slight sunstroke; jaundice; followed by more rapid failure in strength and progressive anæmia; dyspnœa; palpitation; nausea; vomiting; slight œdema; faintness and giddiness on rising; hæmic murmurs; very slight fever; no leukæmia, but extreme anæmia; very slight emaciation; delirium; death. No affection of lymphatic glands; slight enlargement of spleen; fatty degeneration of heart, liver, and kidneys.—W. G., æt. 57 at time of his death, June 12, 1872. He was a native of England, but came to America at the age of 14 years. He was a short, heavily built man of rather sanguine or plethoric constitution. He enjoyed unusually vigorous health, having had no sickness excepting an attack of measles in childhood; and since then having never had occasion to consult a physician until his last illness. He lived continuously in Philadelphia, and both his residence and place of business were in healthy localities. He was not exposed to malaria or to any metallic poison; being engaged at the head of a large wholesale crockery business. He was a very hard worker, frequently being at his store from 8 A.M. to 10 or 12 P.M. He was very successful and made a great deal of money; though he lost much by endorsing. He was never rendered anxious or overstrained; but was always amiable and took the world very easily. He was very domestic in his habits; was married, and had nine children, who all survived him, though subsequently the youngest son died of acute caseous pneumonia. There is not the slightest suspicion of his ever having had syphilis. He was temperate in his habits, eating heartily of simple food, and drinking ale moderately. He had never suffered from chronic diarrhœa.

For two years previously his sons had assumed chief charge of the business, and in consequence he was much less occupied than it was his habit and wish to be; and this enforced idleness after a life of great activity was irksome to him. In July, 1871, while sitting in a chair in the hot sun overseeing some repairs to his store, he had a slight sunstroke or syncopal attack. He grew faint and almost fell from the chair, but recovered in a few hours and did not seem to suffer from it afterwards. His wife states, however, that even for some months before the above attack, she remembers that he would occasionally strike himself over the breast, and cough, saying that there was something there which would eventually cause his death. It is probable that during this time there was a slow and gradual failure in vigour, although he never alluded to any symptom of ill health. In the following March (1872), he began to be jaundiced. The yellowness came on without apparent cause, with no pain or symptom of calculus. The urine was high-coloured, but the feces were not pale. He was constipated, his appetite began to fail, and, though he continued to attend to business, he lost strength rapidly and his flesh failed and grew flabby and soft. After about a month, the yellowness gradually diminished; but left the surface of a deathly pale color, with a tinge of sallowness, strikingly like the colour of a corpse. His weakness increased, but he still continued to attend to business until towards the middle of April, when he fainted in his store and had to be carried home. He then only left his house to drive in the afternoon, but soon after fainted while in his carriage, and thenceforward did not leave his house. His weakness increased so much that during the first week in May he was compelled to go up stairs on his hands and knees, as walking up exhausted him so greatly. He now noticed that any exertion produced great nausea, with retching and vomiting; and indeed, for a couple of weeks after the

development of the peculiar corpse-like appearance, his appetite was lost entirely so that he loathed food and frequently vomited after having forced himself to eat. Greasy food was especially repugnant to him.

I saw him first on May 10th. He was then confined to his bed. He made no complaints of pain in head or elsewhere, nor indeed of anything but constant sense of great weakness. Every exertion, even that of rising in bed, caused great faintness. The entire surface was deathly pale, with a faint sallow, cadaveric hue. The conjunctivæ were pearly white; the mucous membrane of the mouth entirely bloodless. There were no ecchymoses or petechiæ on any part of the surface. Vision was not disturbed, but no ophthalmoscopic examination was made. There was a distinct puffiness of cellular tissue under eyes, but no œdema in any other part. The tongue was intensely pale, moist, and clean. There was no appetite; and food was ill borne, great care being needed to avoid exciting vomiting. The abdomen was rather large and distended with flatus, and was free from any serous effusion. The bowels were quiet and rather costive, but were readily moved by enemata. The movements were small but apparently normal, containing no excess of free fat, and not pale in colour. There never was any hemorrhage from the bowels. The urine was no longer dark-coloured, but was of normal character and entirely free from albumen. There was no pain complained of in abdomen. The liver and spleen were not enlarged or sensitive.

Respirations were quiet, though easily disturbed by any exertion; no cough; physical examination showed that the lungs were entirely healthy. The heart's action was somewhat frequent, when the circulation was quiet; the pulse was about 90, but exertion readily disturbed it. The area of dulness was normal or very slightly increased; the apex beat very feeble; on auscultation no valvular murmur was detected; the first sound was weak and poorly developed; over the base a soft hæmic murmur was audible, which could be traced along the pulmonary artery; no venous hum could be detected in the neck. Microscopic examination of the blood showed no absolute increase in number of white corpuscles, but very advanced decrease in the red corpuscles. The fluid was thin and dirty-red in colour. The record of the temperature has been lost, but it was but slightly above normal.

The treatment ordered consisted of careful alimentation by stomach and rectum; carbonated water, bismuth, soda and creasote mixture at different times to relieve nausea, which was held in check so that vomiting was comparatively rare towards close of life. The following was also administered: *R.* Quinæ sulph. gr. ij; strychniæ sulph. gr. $\frac{1}{40}$; tinct. ferri chloridi, gtt. viij; acid. muriatic. dilut. gtt. v; syr. zingiberis, fʒi; aquæ, fʒiij. *Pt. sol.* S. thrice daily in water. This was well borne for a while; subsequently various changes were made in the form of iron and quinia, but these were the drugs chiefly relied on. Transfusion was not performed. The case was regarded as one of idiopathic anæmia with advanced fatty degeneration of the heart. The jaundice was regarded as having been of hæmic origin.

From this time until death, June 12, 1872, rather more than four weeks later, no marked change occurred in his symptoms. The vomiting was checked, but no appetite returned. The anæmia grew more and more profound. No hemorrhage took place, but examination of the blood showed increasing alteration, but without any increase in the proportion of white corpuscles. There was no improvement in his strength. Towards the

close the feet grew œdematous and a small amount of ascites supervened. Death finally occurred from sheer asthenia, with mild wandering delirium. The degree of loss of flesh remained moderate until the end.

Autopsy.—Intense anæmia as above described. There was very little blood in the vessels, and this was thin and watery, of light dirty-red colour, almost without coagula, even in right side of heart. Microscopic examination gave same results as before.

There was still a considerable amount of adipose tissue in omentum, abdominal walls, and other parts of subcutaneous tissue.

Head.—Brain very pale and bloodless; increase of subarachnoid effusion.

Thorax.—*Lungs* healthy, very pale and anæmic, excepting posterior part of lower lobes, which were œdematous and congested; no pleural effusion; a small amount of clear serum was found in the pericardial cavity; and the surface of the heart presented a number of small ecchymoses. The heart was slightly enlarged; presented a considerable amount of fatty accumulation on its outer surface, and on being removed from the chest was found so flabby and relaxed as not to retain shape at all when laid on a flat surface. Its cavities were slightly dilated, and contained some thin watery blood with a few soft small clots. The muscular tissue was very soft, tore readily, was of a pale yellowish-red colour, and on microscopic examination presented an *extreme degree of fatty degeneration*. The aorta and large veins were healthy.

The liver was of full size, soft, friable, pale and yellowish in patches. Examination showed extreme general fatty degeneration of the tissue. The gall-bladder contained thin pale bile, no calculi. The kidneys were rather large, pale, and very far advanced in fatty degeneration.

The *supra-renal capsules* were of full size, apparently healthy, presenting no characteristic cheesy degeneration.

The *spleen* was somewhat enlarged (half more than natural), its pulp was dark and much softened; no leukæmic lesions present.

The *lymphatic glands* were nowhere involved. The *marrow* of the bones was unfortunately not examined.

The characters of this case are so well marked as to need no comment. At the time that both this and the previous case occurred, no report of the recently observed cases of Gusserow and Biermer had reached my notice, and I find that I have simply headed the latter record with the title "*pernicious anæmia, with fatty degeneration.*" During life, the diagnosis was very obscure, except so far as the cardiac and hæmic lesions were concerned, and so far as an utter absence of the symptoms of organic disease of any other part. The case was regarded as one of acute fatty degeneration, dependent upon primary intense anæmia, and I was inclined to refer the occurrence of jaundice, without apparent cause and followed by such rapid and intense destruction of red globules, to a hæmic origin. The slight sunstroke or syncopal attack cannot, it seems to me, be regarded as in any way the cause of the subsequent cachexia, but as merely a sign of insidious failure in strength and vigour and power of resistance which had previously been slowly progressing. Unfortunately it was impossible to make any special examination of the marrow of the bones. The entire absence of any increase in the number of white corpuscles was repeatedly determined.

In the following case, of recent occurrence, a more minute study of the symptoms and lesions was made; and it will, I trust, prove of interest as showing for the first time, so far as I know, the important fact that this peculiar form of progressive anæmia may be associated with changes in the marrow of the bones such as has been shown to exist in certain cases of leukæmia.

CASE III. *Chronic follicular catarrh; attacks of hepatic colic; mental and bodily overstrain; apparently causeless anæmia and debility; tendency to syncope; transient œdema; hæmic murmurs; dyspnoea; irregular fever; somnolence; transfusion, with temporary relief; increasing debility; ecchymoses; wandering delirium; second transfusion; death in twelve hours. Calculus retained in gall-bladder, with chronic suppuration of the sac; enlargement of solitary follicles of intestines; intense anæmia; fatty degeneration of heart, liver, and kidneys; slight swelling of spleen; no affection of lymphatic glands; marked affection of medulla of bones.*—E. C., æt. 50, engaged in iron founding. He and his brother have worked intensely hard, elaborating patents and carrying heavy business cares. He always discharged the financial part of the business. A man of rather spare frame, never weighing over 130, lithe and active in body and mind. Never enjoyed what could be called vigorous health. At age of twenty-five years he had a very severe attack, attended with vomiting, pain in right hypochondrium, but with no jaundice. Since then he has never been so well as previously, but every year or two has had a similar but less severe attack. In no case did jaundice follow. There has been, besides, a weak condition of the bowels ever since, the stools being habitually undigested and thin, though rarely amounting to more than one a day. No distinct account can be had of any hemorrhage from the bowel having occurred. He suffered for many years (twelve to fifteen) from an obstinate form of psoriasis, chiefly affecting legs, and to a less extent the arms and trunk. These affections did not diminish his energy and activity. He lost nearly all of his upper teeth twelve to fifteen years ago, and could not be induced to wear false ones, so that this must have aided in interfering with his nutrition by preventing complete mastication. He was married, and had a healthy family. He was strictly temperate in every respect, and resided in a healthy suburb of Philadelphia.

He seemed in his usual health till the early part of February, 1875, although subjected to unusually severe strain during the past two years of business depression. About the tenth of that month he did an unusually hard day's work, and noticed next morning that he was feeling poorly and weak. He consulted his sister, Dr. Hannah T. Croasdale, who prescribed rest and tonics. However he continued as usual at his business until early in April, when his debility had become so extreme that he was compelled to remain in his chamber. For some short time before this, he noticed shortness of breath on exertion; and on April 10, there was a rather abrupt appearance of œdema of face and extremities. There had been no diarrhœa or hemorrhage, or exhausting influence of any kind to produce this steady increase in prostration. At the same time, an alarming state of pallor of surface developed itself, the skin becoming excessively pale, with a faint sallow tinge. After the occurrence of the œdema he remained for the most part in bed until his death. The swelling rapidly disappeared, and there was no return of it subsequently. He continued able to take nourishment naturally; was free from suffering, and took interest in everything, retaining his faculties perfectly.

During this time he took iron in various forms and in quite large doses, but it did not seem to agree with him; his stools being very black and his appetite failing. The heart's action was feeble, with occasional intermissions; and a strong hæmic murmur was heard over the base. The pulse was weak—not much accelerated. No record of bodily temperature was made; it is probable that he had slight irregular fever. There was no vomiting. He also had two short attacks of pain in right hypochondrium, with nausea. His ability to take food steadily declined, and latterly he was obliged to be nourished in great part by enemata of beef extract.

I first saw the patient April 30, 1875, in consultation with Dr. Charles H. Thomas and the patient's sister, Dr. H. T. Croasdale, at 12 o'clock noon. A few hours previously he had been subjected to some exertion—having his clothes carefully changed and being gently carried from one room to the next. This was followed by dangerous syncope—entire unconsciousness lasting for a moment. Brandy was given in small quantities every 20 or 30 minutes, and he gradually rallied to a slight degree. He was found lying in bed with his head slightly lowered. His facies was strictly corpse-like—deathly pale, with a trace of sallowness—but without a vestige of healthy colour. Conjunctivæ pearly white; lips blanched; gums bloodless; tongue dry, very pale, coated on dorsum. No coolness of surface. Lies with eyes closed, and dozes constantly; can be readily aroused, and opens eyes, looks intelligently, understands, and answers clearly. Has sense of intense weakness; and this is so much aggravated after sleep that he is afraid to sleep more than a few minutes, and is accordingly awakened every 30 minutes.

Respirations are regular, quiet, with healthy vesicular murmur; pulmonary resonance unusually marked. Pulse weak, quick, compressible, 96 to 102 in minute, somewhat irregular, with occasional intermissions (1 to 3 in every minute). Heart's action similar; soft, musical, hæmic murmur at base, heard along pulmonary artery and less strongly over aorta; no venous hum in neck; no murmur heard on auscultating head. No emaciation, the degree of flesh being very little less than when in ordinary health.

There is no œdema of any part. No petechiæ or ecchymoses.

Abdomen normal; no ascites; liver not enlarged, nor sensitive; spleen slightly enlarged. Nausea and vomiting provoked by any exertion. Frequent administration of small quantities of brandy was directed, together with beef extract by enema.

Transfusion was recommended without delay, and at 6.30 P. M., same day, was performed by Drs. T. G. Morton and C. T. Hunter.

At 6.25, just before operation. Pulse 98, 2 intermissions in minute; temperature in right axilla 101° F. Microscopic examination of blood showed no real excess of white corpuscles, but some relative excess in consequence of extreme reduction in number of red globules; there was but little formation of rouleaux; the individual corpuscles seemed pale, and less biconcave than normal; no abnormal elements were seen. The power used was a Tolles' one-fourth inch.

His brother furnished the blood, which was carefully defibrinated, and $\frac{1}{2}$ iijss slowly injected into right median basilic vein. The operation was effected without the least inconvenience. During entrance of blood there was at first some increased frequency of pulse to 108, but it then fell to 90, becoming stronger and fuller, and losing the intermissions. He experienced some sense of increased strength; but no change occurred in his appearance.

At 7.30 P. M., one hour afterwards, he complained of chilly sensations

("creeps") along spine—succeeded at 7.45 by free vomiting and copious and repeated involuntary evacuations of the bowels, with abdominal pain. The pulse rapidly increased in frequency to 120, becoming much weaker and markedly irregular, and the surface grew much hotter. *Sp. ammoniæ aromat.* and brandy were given, and hot-water bottles placed around him, with but slight effect. At 8.30 a suppository containing *morphiæ sulph.* gr. $\frac{1}{4}$ was given.

At 9 P. M., abdominal pain relieved; necessary to keep windows wide open to furnish air; temperature in right axilla $104\frac{1}{4}^{\circ}$ F.; pulse 128, weak and compressible, and intermittent; skin moist.

By 11.30 P. M., the pulse had fallen to 100, still weak and intermittent. May 1, 1875. At 1 A. M., pulse 104; respiration 20; temperature 101° .

At 2.30 A. M., pulse 92, 2 intermissions.

At 5 A. M., pulse 90, full and regular—no intermission; temperature 100° . During night he slept, being awakened every half hour to avoid excessive depression. At 4 A. M., he said he felt undoubtedly better. He took brandy and water every half hour, and a small amount of beef extract by mouth. No enemata were given. The pulse lost somewhat in volume in early morning, and one or two intermissions were noted in each minute.

The first urine voided after the transfusion was unavoidably lost; and it was not examined until early on morning of 2d, when it was found clear and amber-coloured, sp. gr. 1018, free from albumen.

During the remainder of the day, there was steady and decided improvement, as may be seen by following record:—

	Pulse.	Respiration.	Temp.
At 11.30 A. M.	96, 2 intermissions,	18	101°
3 P. M.	98, no intermissions,	18	
6 P. M.	88, no intermissions,	18	101°

During this day, he was nourished by the whites of uncooked eggs (of which five were taken) stirred with brandy and water, to which occasionally a little cream was added; and enemata of beef-tea with a few drops of laudanum. The entire amount of brandy taken in last twenty-four hours was $\text{f}\overline{\text{3}}\text{ij}$. Elix. bismuth, pepsin, and strychnia in $\text{f}\overline{\text{3}}\text{j}$ doses was given five times a day.

2d. Had passed a good night, sleeping nearly two hours at a time. His pulse was of fair volume, without intermissions, and varied from 93 to 97; respirations were regular, and continued at 20 in the minute; temperature at midnight was $100\frac{1}{2}^{\circ}$; at 6 A. M., 99° ; at 3 P. M., $99\frac{3}{4}^{\circ}$. He urinated quite freely; the secretion was clear and free from albumen, but was not examined microscopically. His intellect was clear, and he expressed himself as feeling stronger. There was still extreme desire for fresh cold air, so that all the windows in his room were kept open day and night. He complained of no pain. No petechiæ or hemorrhages. He took food as on previous day, and without nausea or vomiting. Bowels quiet; rectum retentive; enemata of beef juice $\text{f}\overline{\text{3}}\text{ij}$, tr. opii. gtt. vi, quiniæ sulph. gr. iv, given three or four times in twenty-four hours.

3d. General condition seemed slightly more favourable. He slept better and with less exhaustion. Bowels opened spontaneously and naturally. Took nourishment more willingly; and also retained the enemata of beef-tea. Pulse continued about 96, without intermission; temperature varied from $98\frac{1}{2}^{\circ}$ to 100° . No positive diminution in degree of anæmia.

4th. Did not seem quite so well. Had passed a fair night, but was rather weak and chilly this morning; still craved fresh air and felt faint if

the windows were closed at all. Pulse varied from 95 to 100, and again presented one intermission in each minute; temperature 99°. Less relish for food. Tongue more thickly coated, and brownish and dry on centre of dorsum; anæmia intense. Same nourishment was continued; with enemata as before. He was now ordered tr. ferri chloridi, gtt. iij, liq. pepsin, f5j, t. d. after meals, in place of the elixir he had been using.

5th. A marked change in weather had occurred, and it was thought he had taken cold in consequence. He seemed decidedly less well, and had greater sense of prostration. Pulse had risen to 106 or 108, was less full, and extremely feeble; respirations had risen to 25; temperature rose from 101 $\frac{1}{2}$ ° at 8 A. M., to 103 $\frac{2}{5}$ ° at 8 P. M. He urinated more frequently—about every two hours—but none was secured for examination; bowels quiet. The same nourishment (raw eggs, cream, and brandy; milk and lime water; beef-juice) was continued, but the amount of brandy was increased by adding half fluidounce to each enema; the amount of quinia by enema was increased to gr. xvi daily, and tr. digitalis gtt. viij every four hours was substituted for the iron. There was no cough or sign of pulmonary trouble. The anæmic heart-murmur was distinct. The tongue continued brownish and dry. He was also ordered a suppository of morphia gr. one-eighth at night.

6th. The febrile exacerbation seems to have diminished, the pulse still somewhat accelerated, 100 to 102. Has had a very comfortable night, and feels refreshed. General condition much the same. Tongue has quite thick brownish coating in centre. No appetite, but no nausea or vomiting. Loathes alcohol. Has had natural, spontaneous movement of the bowels. A slight livid appearance was noted this morning in face. It was decided to repeat the transfusion, and at 12.40, f5jvss defibrinated blood was injected by Drs. T. G. Morton and C. T. Hunter into *lef?* median basilic vein at bend of elbow. Dr. S. Weir Mitchell was also present, and kindly assisted in making the observations on the pulse during the operation. Just before operation temperature was 101 $\frac{1}{2}$ °; pulse had risen from excitement from 108 to 120, not intermittent.

During injection of first syringe-ful, pulse remained 120, but grew intermittent, losing three or four beats in minute.

During injection of second syringe-ful, pulse rose during first quarter of minute to 33; and during second quarter to 35.

After the injection of three syringe-fuls a pause was made for about two or three minutes, during which pulse rapidly fell to 108 per minute.

The third syringe-ful was injected very slowly, occupying just one minute; during this the pulse was in the successive quarters, 28, 27, 28, 28; and during injection of fourth syringe-ful, 29, 29, 27, 27.

The operation was accomplished without pain or discomfort to the patient. As soon as it was over he said he was glad it had been done, and that he felt a little stronger. No perceptible change in appearance. Pulse continued to fall to 100, and then in course of thirty minutes was 104, with one or two intermissions.

At 1.30, very soon after the operation, nausea began, and he soon vomited; at same time there was rumbling in bowels, with involuntary discharge of fluid feces. These symptoms at first seemed much less severe than after the first transfusion. But in a short time the pulse and temperature began to rise (see table); his color grew livid, with great restlessness and complaints of pain in the head. This restlessness increased, and was very distressing from two until six o'clock, with constant tossing of hands about, although prostration was evidently steadily increasing. Later he grew more quiet, and at 9.30 he was unconscious.

Date.	Hour.	Pulse.	Res. Temp. F.	Remarks.
1875. Apr. 30	12 noon	96-102, intermittent	20	
	6 P. M.	98, intermittent	... 101°	Transfused f3ivss at 6.25 P.M.
	9 P. M.	128, interm't & feeble	... 104 $\frac{1}{2}$	Probably higher about 8 P.M., but not observed.
	11.30 P. M.	100, intermittent	20 ...	Temperature falling.
May 1	1 A. M.	104, intermittent	20 101	
	2.30 A. M.	92, intermittent	... 100	
	5 A. M.	90, regular, more full	... 101	
	11.30 A. M.	96, intermittent	18 101	
	3 P. M.	98, regular	18 101	
	6 P. M.	88, regular	18 101	
	12 midnight	94, regular	20 100 $\frac{1}{2}$	
May 2	6 A. M.	96, regular	20 99	
	3 P. M.	96	20 99 $\frac{3}{5}$	Condition comfortable.
	12 mfdnight	96, intermittent	20 98 $\frac{3}{5}$	
May 3	9 A. M.	90, intermittent	18 99	
	6 P. M.	96, regular	20 100	Condition very satisfactory.
	12 midnight	96, regular	...	
May 4	3 A. M.	100, feeble	20	
	6 A. M.	98	20 99 $\frac{2}{5}$	
	12 noon	94, intermittent	18 99	
	6 P. M.	100, regular, weak	20	
	11 P. M.	Feels chilly.
May 5	1 A. M.	107, very feeble	...	
	4 A. M.	107, extremely weak	...	
	8 A. M.	106, a little stronger	24 101 $\frac{1}{2}$	Increased febrile action; or- dered digitalis, and in- creased amount of quinia.
	8 P. M.	108, regular	... 103 $\frac{2}{5}$	
May 6	5 A. M.	100, regular	18 100	
	10 A. M.	102	... 101	
	12.50	129	... 101 $\frac{2}{5}$	At 12.50 transfused f3vss bl'd.
	2.15 P. M.	120	... 104	Vomiting and purging at 1.30 P. M.; lividity.
	3 P. M.	150, intermittent	24 ...	Complains of pain in head.
	4.15 P. M.	124	... 103 $\frac{1}{2}$	Very restless from 2 until 6, tossing arms about, etc.; after that unconscious.
	5.30 P. M.	128	... 104 $\frac{1}{5}$	
	6.45 P. M.	119	... 104	
	8.30 P. M.	120	16 103 $\frac{2}{5}$	
	9.30 P. M.	130	18 105	
	10.30 P. M.	120	15 105	
	12 midnight	120	18 106	
May 7	1 A. M.	124	13	
	2 A. M.	140	11	
	3 A. M.	Expired.

A suppository of morphia gr. one-eighth was ordered just before the operation; but by accident suppositories containing gr. one-fourth had
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been substituted for them, and one was administered at 12.20, 1.45, and 3 o'clock. No further evacuations occurred. At 3 A. M., May 7th, he quietly expired.

In morning of this day, May 6th, some hours *before* transfusion was performed, the minute petechiæ described in post-mortem account made their appearance; but the nurse did not call attention to them.

It is doubtful if the morphia had any influence upon the results of this second transfusion. The amount taken was not large (only 1 grain in all), and the symptoms, excepting the relative slowness of breathing, were such as are frequently observed before death after transfusion.

Post-mortem Examination.—The body did not present the slightest evidences externally of decomposition, nor was there any odour to indicate it. The surface was intensely pale. Over the shoulders and the front of the chest and trunk, there were numerous minute petechiæ; a few very small ones were also seen on humeral regions and thighs. There was no œdema of any part of the body; over the legs, and to a less extent on the arms there were still to be found traces of an old eruption, in oval or reddish patches of various sizes where the skin is dry, irregularly thickened and covered with shining scales (psoriasis). There was a fair amount of fat in the subcutaneous tissues as well as on the omentum, the pericardium, and diaphragm.

Thorax.—The costal cartilages were very firmly ossified. The cartilage cells exhibited no disposition to proliferation, but many of them contained more than the usual amount of oil in small and large drops. There were about four fluidounces of reddish serum, like claret and water, in the left pleural sac, and about two ounces on the right side. There were a few slight adhesions over apices of lungs. The anterior parts of the lungs were anæmic and pale, while the posterior portions were dark, congested, and œdematous. No ecchymoses or spots of infarction were found.

The pericardium was apparently healthy, and not stained by imbibition; it contained one fluidounce of bloody serum, which showed under microscope a few epithelial cells from the serous membrane, and a very few red globules, very faintly visible. On cutting the vessels of the heart, soft, dark clots escaped from the aorta, pulmonary artery, right auricle, and vena cava. The lining membrane of heart and great vessels was deeply stained. The right ventricle contained a moderate amount of dark, partly fluid blood, which was beginning to decompose and contained minute bubbles of gas; the left ventricle was almost entirely empty. The heart was so flabby that it did not retain its shape in the slightest degree when placed on a flat surface. The muscular structure was very soft, friable, and pale. The walls of the right ventricle were thinned, and especially soft and pale. There was no valvular lesion. The aorta showed a few small patches of atheroma. Fragments from wall of right ventricle showed under microscope, not much free interstitial oil, but almost entire loss of striation; only in a very few fibres could a trace be detected, while the vast majority were in a state of advanced granular and fatty change. The fibres were very friable, and were broken in very small fragments in teasing them out.

Fragments from wall of left ventricle, from small trabeculæ, and from septum ventriculorum, all showed same extreme degree of degeneration.

Blood.—*Clot from right auricle:* fibrin well clotted, but, at first sight, apparent absence of red corpuscles; almost normal number of white corpuscles were seen, revealing normal nuclei on treatment with acetic acid.

On very careful focussing with quite high power (one-tenth) it was seen that the red globules were indistinctly visible, appearing as faint shadows, as though almost entirely dissolved in the serum. Not a single red corpuscle could be found which was distinct.

From Portal Vein: about f3ij drawn directly into clean silver spoon and placed directly in small bottle. Eleven hours later no clot had formed. On looking at drop under glass, a moderate number of white corpuscles and a few filaments of fibrin were visible, but at first no red globules. A misty appearance was observed all over field, which was cleared away by acetic acid, and by careful focussing with a one-tenth Tolles' could be resolved into very faint, almost indistinguishable red globules.

The *liver* was of normal size; its surface was quite pale, except where stained from contact with the colon, and also presented irregular patches of very light yellowish colour. Its veins contained a fair amount of dark fluid blood. The liver substance was fatty to a considerable degree. There was a good deal of free oil in small and large globules. A good many cells were stuffed with oil globules, but in many others the contents were merely strongly granular and the nucleus could be seen. No appearance of disintegration of cells. Some small dark masses, like aggregations of pigment granules, were seen.

The *gall-bladder* was much contracted, not having capacity of more than f3ij or f3iij; its walls thickened and fibrous. The mucous membrane presented a few small ecchymoses, but was smooth and not ulcerated. It contained a rounded blackish calculus, over one-half inch in diameter, and about two fluidrachms of thick puriform fluid, which presented none of the microscopic elements of bile, but abundant cylindrical epithelium, and very numerous pus corpuscles (granular nucleated leucocytes) closely resembling the medium-sized cells found in the marrow. The *bile-ducts* throughout the liver contained pale, but apparently healthy bile. There was no obstruction of the cystic or common duct.

The *stomach* was of ordinary size, the mucous membrane pale, and showing a few small ecchymoses, but otherwise healthy.

The *spleen* was slightly enlarged; the corpuscles healthy; on handling it, distinct crepitation was perceived, owing to decomposition of its tissues, despite the general good preservation of the corpse. The splenic pulp was softened and purplish, without any leukæmic patches or enlarged Malpighian corpuscles. Under the microscope the field was crowded with small round cells (smaller than the majority of the cells in the marrow), spindle-shaped cells, and very pale red blood globules.

The *supra-renal* capsules presented no special change; the central cavities seemed somewhat too large.

Kidneys.—Capsules healthy; tissue intensely pale and softened; cortex not diminished; tissue opaque and cloudy; epithelium very fatty and granular; many tubules choked with fatty epithelial cells or granulo-fatty detritus; no increase of interstitial tissue.

Urine.—No blood globules; numerous large crystals of uric acid, and quite numerous hyaline casts with a few epithelial elements contained; in some cases, also, granular collections in the casts. In one instance a tube cast composed entirely of fatty epithelial cells was seen. Urine highly albuminous. It was the first urine passed after the second transfusion.

The *pancreas* was of normal size, extremely pale, but apparently healthy. Its tissue showed under the microscope quite abundant free oil, with a granular condition of the cells, but without any excess of connective tissue.

Small Intestines.—The walls were thin, pale, and softened; the mucous membrane was pale and especially thin. There was no enlargement of Peyer's patches, but the solitary glands throughout the small intestine, and especially in the ileum, were enlarged and prominent, showing chronic follicular irritation. There was no disease of the large intestine. The mesenteric glands were not materially enlarged.

The *general muscular system* was fairly developed, and was of natural colour and consistence. Microscopic examination of fibres from muscles of forearm showed a healthy condition.

There was a most singular absence of *blood* in all parts of the body (excepting posterior parts of lungs, right side of heart, and veins of liver), so that the remainder of examination was almost unattended with any escape of blood, even after the abdominal vessels were freely opened.

The *brain* was large, with some excess of subarachnoid effusion. The gray substance was very pale: the medulla entirely anæmic. The Pacchionian bodies were large.

Marrow from canal of radius appeared decidedly paler than in health; examined in fresh condition it was found to be made up almost entirely of granular cells, round or nearly so, but varying in size from a diameter of $\frac{1}{80}$ to that of $\frac{1}{20}$ of an inch. Many of the larger of these cells exhibited a single distinct spherical nucleus without the aid of reagents. The smaller cells often failed to exhibit such nucleus before addition of acetic acid, after which, however, as a rule, it was distinctly displayed. A few of these cells also were granular to a marked degree, and a smaller number contained a single drop of fat. There was also a very moderate amount of free oil in large drops.

Marrow from sternum quite red; very little oil; made up of crowded cells, roundish and granular; on treatment with acetic acid, showing in most cases a single round faintly granular nucleus; the cells varying in size from less than a white blood cell to twice that size, the smaller ones preponderating.

It is evident, on reading these cases, two of which were observed without any knowledge of the reports of similar cases, and on comparing them with these reports, that we have to do with a very definite and well-marked condition of disease—not at all new, because it was clearly recognized by Addison under the name of “idiopathic anæmia,” and because it is certain that isolated cases have been observed by different authors; but more distinctly and minutely described of late in consequence of our greater knowledge of diagnosis, and particularly of the distinctive features of the various cachexias.

Like all analogous diseases, this peculiar form of anæmia is not limited to either *sex* or to any *age*. The recent German observers found it more frequent in women, but two of the cases which I have observed were in men. Addison speaks of it as occurring generally, but not exclusively, beyond the middle period of life. Biermer's cases ranged between 18 and 52 years of age; Immerman's were 18 and 31 years old respectively; Gusserow's five patients were from 24 to 36 years old; and in my own cases, the age was respectively 26, 50, and 57 years. If age has any influence upon the production of this affection, which seems to me doubtful,

it may be that, excepting in cases developed in connection with pregnancy, it is more apt to occur about the middle period of life.

As so many cases were observed in the course of a few years at Basle and Zurich, Immerman (*loc. cit.*) suggested that there might be some local cause to explain this rare form of anæmia; but this idea is clearly disproved by the occurrence of similar cases at Dresden, Bologna, in this country, and elsewhere.

Pregnancy would certainly seem to act as a predisposing cause. Gusserow described his cases under the title of "very intense anæmia of pregnant women." Although it is met with in men and non-parturient women, a large proportion of cases so far observed have been in connection with pregnancy, and especially when there have been frequently repeated previous pregnancies. Thus in Corrazza's case there had been four pregnancies in five years; Biermer noted that child-bearing appeared to have acted as a predisposing cause; in one of Gusserow's cases there had been six children born in nine years; in another case, seven children in twelve years; in another, the patient, twenty-nine years old, was in her sixth pregnancy; in another, the patient, twenty-nine years old, was in her tenth pregnancy, having given birth to nine healthy children in nine years. In but one of his cases was the patient a primipara, and in that instance there were extreme over-fatigue, anxiety, and privation in addition. Long ago Cazeaux¹ contended for the existence of a marked tendency to anæmia during pregnancy; and when we consider the profound nutritive changes which attend that state, and the heavy demand which is made upon the maternal system, it is not difficult to understand that when repeated with excessive frequency and rapidity, or if accompanied by depressing influences, a grave and even fatal disturbance of the blood-making function might result. It is, in this way, that it is not uncommon to observe not only the form of anæmia we are considering, but all of the cachexiæ originating in connection with pregnancy.

Another influence which I am disposed to recognize as an occasional predisposing cause is that of a *long-continued local irritation*, especially if associated with mucous or purulent discharge. It will be remembered that Trousseau (*Clinical Medicine*, Syd. Soc. Ed., vol. v. p. 206) endeavours to connect the closely-analogous condition of *adenia* or *lymphatic anæmia* with some previous local irritation. In a considerable number of the cases of so-called progressive pernicious anæmia, chronic diarrhœa, dependent on follicular irritation of the intestines, is reported to have existed before the development of the disease. In the first case here reported, an obstinate bronchial catarrh of five months' duration preceded the appearance of the characteristic symptoms. In the third case, chronic suppuration of the gall-bladder, with chronic follicular catarrh of the intestines, had ex-

¹ *Revue Médicale*, 1851, p. 553, *et al.*

isted for many years. It is evident that this latter cause might operate by interfering with the proper absorption of alimentary matters, and thus gradually undermining nutrition until some grave lesion of a part of the blood-making apparatus was superinduced. There are, however, other cases where no such cause can be assigned, and where the only influence that can be suggested as a possible cause is either overstrain of mind and body, or unfavourable hygienic conditions.

It seems, too, that in some instances chronic syphilis, and possibly chronic malaria also, may so profoundly affect the blood-making tissues as to develop fatal progressive anæmia.

And finally, cases have been met with where no cause whatever could be assigned, and the disease would appear to have originated idiopathically.

The *course* of the disease has been unusually similar in the majority of recorded cases, and in most respects the graphic description of Addison (p. 316) might still serve. Sometimes there is an indefinite period of slight failing in health before any change in appearance is observed; in other cases the patient complains of a gradual and increasing pallor, with loss of strength. More rarely the patient can refer to some particular week or day as marking a more abrupt beginning of his sickness.

The *appearance* of the patient soon becomes characteristic of extreme anæmia. In a small proportion of cases, jaundice of quite marked intensity may occur (Corrazza's Case, and Case II., here reported), and then subsequently the skin may retain a faint straw-coloured tint. But generally the surface is deathly pale, with or without a faint tinge of sallowness, the conjunctivæ pearly white, and, towards the latter stage of the disease, the bloodless pallor of the skin and mucous membranes is greater than I have ever seen it in other conditions, and the appearance of the patient becomes frightfully corpse-like. No abnormal pigmentation occurs.

Dropsy is a very frequent symptom, both as œdema and in the form of internal serous effusions. The œdema may be slight and transient, as in Case II. and III., or it may be persistent; in the latter form it usually comes on late in the case. In Case I., after having been limited to the face and ankles, it rapidly increased and spread over the whole body shortly before death. In Case II. it was limited to puffiness under the eyes, such as is so often seen in latent renal disease. It is evidently due to the watery condition of the blood, aided by the feeble state of the circulation. Internal effusions are frequent, but occur late, and are rarely of sufficient extent to attract notice by any special symptoms during life.

Emaciation does not occur to any marked extent. Addison laid especial stress upon the maintenance of the bulk of the frame, despite the utter exhaustion; and although in many cases a moderate amount of loss of flesh occurs, it is not to be compared with the emaciation which attends many exhausting diseases.

The *nervous symptoms* which are present are to be attributed chiefly to

the deficiency of blood and the weakness of the circulation. At first there is merely a sense of languor and indisposition to exertion; later the patient complains of giddiness and faintness, even upon sitting up; the mind grows dull, or can be fixed upon any subject but for a short time; somnolence increases with or without occasional wandering delirium, and as death approaches there may be deepening coma, or delirium may still persist. The patient also complains of the most intense feeling of muscular weakness, and this is frequently the only symptom that will be referred to by him. In my own last case this sense of prostration was so profound that the patient continually believed that he was about to die; and so terrible was it on awakening from sound sleep, that he insisted upon being disturbed every half hour. This is clearly suggestive of the anæmic state of the nerve-centres. Biermer noticed in some of his cases that transient paralysis occurred, which he attributed, with apparent reason, to small hemorrhages into the brain-substance.

The *circulatory* disturbances, intimately connected as they are with the state of the blood, are very interesting. The pulse is accelerated, and is very readily affected by trifling effort or excitement. Early in the disease it may retain a fair volume, but later grows small; it is always weak, compressible, or even gaseous. In addition it may, as in Case III., be intermittent. The patient is subject, from an early period of the case, to spells of palpitation, which may occur without apparent cause, but are usually the result of slight excitement or of some exertion, such as going up stairs, or even rising in bed. A marked tendency to attacks of syncope is a nearly constant symptom, and so dangerous may these be, as in Case III., that it is evident that any considerable effort should be avoided lest sudden death may occur.

The heart's action is feeble, the impulse very weak, and the sounds, especially the first, are poorly developed. When to these characters are joined the acceleration of action, the tendency to palpitation, the occasional irregularity or intermission, and the character of the pulse, it will be seen that the physical signs of marked fatty degeneration are distinctly present. Added to these are unusually strong hæmic blowing murmurs. In some cases these are limited to the region of the heart, aorta, and pulmonary artery, where they may be soft, or so loud and strong as to raise suspicion of the presence of organic disease. In other cases, as in Case I., there is associated with the hæmic cardiac murmurs, a well-marked anæmic hum (*bruit du diable*) in the large veins, especially the jugulars. I would allude particularly to the subjective roaring heard by the patient herself in that case, and to the fact that a distinct continuous humming murmur, uninfluenced by respiration, was audible on auscultation over the whole skull, and especially over the course of the lateral and longitudinal sinuses. In one of Gusserow's cases venous pulsation in the neck was observed.

The tendency to *hemorrhage* varies much in different cases. Thus in Case II. no hemorrhage occurred during life, and at the autopsy ecchymoses were found only on the visceral layer of pericardium. In Case III., the only hemorrhage noticed during life were numerous small petechiæ on the last day, and subsequently ecchymoses were found only under the mucous membrane of the stomach. In Case I., on the other hand, there was repeated hemorrhage from the gums, and menstruation was excessive. In many of the cases recorded abroad, petechiæ occurred—under the skin or in the retina—and occasionally hemorrhage took place from the nose or kidneys, or into the brain. No ophthalmoscopic examination was made in any of the cases here reported. It is possible that the coma which appeared before death in Case I. may have been due to cerebral hemorrhage. On the whole, hemorrhage in some form is a frequent and characteristic, though by no means constant, symptom; it occurs in many different forms, usually towards the close of the case, and in connection with internal organs is very frequently found among the post-mortem lesions.

In no case which presents the above symptoms, should we omit to make a most careful examination of the *state of the blood*. It is evident from a glance at the patient that the mass of the blood is diminished to an extraordinary degree, and this is confirmed by post-mortem examination. (See pages 324 and 332). A drop of blood drawn by pricking the finger seems thin and of a light dirty-red colour. Microscopic examination shows that the white corpuscles have undergone no increase whatever, though owing to the great diminution in the red globules, their relative proportion may seem somewhat increased. No peculiar change in the white corpuscles has yet been observed. The most striking change, however, is in the red globules. I do not know of any careful analysis to show how far their proportion is reduced, but it seemed to me I had never looked at a microscopic field of blood where the diminution in red globules even approached what was observed in Case III. No rouleaux were found, and the globules seemed paler and less biconcave than normal.

The *respiration* is naturally much disturbed, although no pulmonary lesion is present. With the attacks of palpitation above described, there is paroxysmal dyspnoea, and after the disease is fully established the breathing is very readily disturbed by slight exertion. Still later, when the anæmia is far advanced, I have noticed a peculiar persistent sense of insufficient aeration, which was so intense in Case III. that the patient insisted upon all the doors and windows of his bed-chamber being open, though the draft which was caused was so cold and strong that his nurses had to wrap themselves in fur robes during the night-watches. There is usually no cough, though in the latter stage of the affection, owing to the development of œdema and congestion of the lower lobes of the lungs, the breathing is apt to be quickened, and dry cough may appear. Physical examination in no case revealed any abnormal sign, excepting ex-

aggregated pulmonary resonance, owing to excessive anæmia of the lung tissue; until towards the close of the case, when congestion of the lower lobes appeared, with feeble vesicular murmur and subcrepitant râle.

The *digestive* system affords symptoms which are quite constant though not characteristic. I have already alluded to the fact that in a considerable proportion of cases the patient has previously suffered from chronic diarrhœa; but whether this has been so or not, there is apt to be occasional diarrhœa during the course of the disease, and especially towards its close. In some cases, on the other hand, the bowels are quiet throughout. I am not aware that hemorrhage from the bowels has yet been observed, though it may be expected to occur in some cases. The tongue is extremely pale; it may remain clear and moist, or, again, may present, as in Case III., a heavy whitish or yellowish fur. The appetite fails, and there may be entire anorexia; in some cases there is actual loathing for certain kinds of food, as greasy substances. There is usually a feeling of weight or pressure at the epigastrium, which is increased by food. Nausea is easily excited; in my own cases slight exertion was sufficient to produce it, and even to cause retching and vomiting. The abdomen is entirely indolent, is apt to be rather large and distended from the presence of flatus, and towards the close of the case often presents a moderate amount of peritoneal effusion (ascites).

The *liver* does not appear to be specially affected. In Case III. there had been attacks of hepatic colic for years previously, but the symptoms of the intense anæmia which developed itself later were not modified by hepatic disturbance. The jaundice which occasionally occurs, as in Case II., is transient and does not seem to depend upon any organic change in the liver, but to be due either to catarrhal inflammation of the ducts, or, as appears more probable to me, to the acute alteration of the blood. It will be noticed that both in Corrazza's case and my own the jaundice occurred early in the case, and upon its subsidence the evidences of intense anæmia were manifest. Throughout the disease (even in Case II., where the jaundice was most marked) the stools were well coloured.

The *spleen* is almost always enlarged, though but so moderately that it is frequently impossible to demonstrate the fact by percussion or palpation during life. The characters of the organ will be described further on, when speaking of the morbid anatomy of the disease.

The *lymphatic glands* are not at all enlarged.

The *urine* is, as a rule, normal in quantity and quality. In a few cases a small amount of albumen has been detected, though without the presence of tube-casts. In none of the three cases I have reported was albuminuria present, with the exception of the urine passed in Case III., soon after the second transfusion, which contained a large amount of albumen with hyaline and granular epithelial tube-casts. Although there was marked fatty degeneration of the kidneys, however, it is evident that this

was to be attributed to the effects of the transfusion, as the urine had been repeatedly examined previously without detecting any albumen. In a few of the cases reported abroad, hemorrhage from the kidneys is stated to have occurred.

There is no reason to suspect the *pancreas* of being implicated. In two of my cases careful examination of the stools failed to show any excess of free oil.

It remains only to notice the fact that throughout the course of this affection there is a tendency to *febrile action of irregular type*. In some cases this occurs in rather a paroxysmal way, the temperature being almost normal for a time, and then quite decided febrile exacerbation manifesting itself, and again subsiding after a few days. In other cases there is more continuous though still very irregular febrile movement. The elevation of temperature usually shows itself towards evening, as in hectic fever; and at times, as in Case I., the periodicity is so well marked as to arouse suspicions of the malarial nature of the case. The usual range of temperature is from the normal point to 101° or 102° ; but it is recorded in some cases as high as 103° and 104° . In the table appended to Case III., it will be seen that the temperature, which, before the first transfusion, was slightly elevated, 101° , immediately afterwards rose to $104\frac{1}{4}^{\circ}$, then rapidly fell again, and remained about normal for a few days, when a fresh rise began, the temperature reaching $103\frac{2}{3}^{\circ}$, and falling again during the night. Even before the second transfusion it was again rising, but under the effects of that operation it rose with frightful rapidity in twelve hours to 106° , when death occurred. Although this tendency to irregular febrile action is an important symptom, it cannot be spoken of as constant, and in some cases it is probable that the disease may run its entire course without any positive elevation of temperature.

Having thus alluded to the most important symptoms, a brief allusion must be made to the *morbid anatomy*.

The most remarkable changes are those connected with the *blood*. In the first place, the entire mass of the circulatory fluid is reduced to a greater degree than I have ever before witnessed, so that not only are all the tissues remarkably bloodless, but even the veins appear almost empty. In both of the examinations I have made, it is no exaggeration to state that after the escape of a small amount of blood from the portal vein, the remaining abdominal veins were literally empty. The characters of the blood have greatly changed. There are soft, dark coagula in the cavities of the heart, but elsewhere the blood shows little tendency to coagulate. Its colour is a dingy, dirty red (like thin coffee—Gusserow); it is very thin and watery, and is prone to undergo decomposition. I have already alluded to the microscopic appearances, and will merely add that in Case III., although it is probable that these appearances were in part due to the fatal effects of the second transfusion, the blood presented a truly

remarkable condition of the red globules, which were so pale and indistinct, as if from solution in the serum, that it was only by delicate focussing and the use of high powers ($\frac{1}{10}$ objective, Tolles) that they could even be detected as faint, shadowy outlines.

Nervous System.—The only constant appearance here is that of extreme anæmia of the membranes and substance of the brain. There may also be the traces of minute hemorrhages into the cerebral tissue. Frequently there is a rather unusual amount of clear serous effusion at the base. I am not aware that any microscopic examination has been made, excepting that by Mr. Quekett of the sympathetic ganglia, which are reported by Addison to have been fatty.

Circulatory System.—Next to the changes in the blood, the most constant lesion hitherto found is fatty degeneration of the muscular tissue of the heart. This may involve the entire substance of the heart, leading to loss of striation of the muscular fibres, and accumulation of fatty granules and minute oil-drops within the myolemma; or, as in many of Biermer's cases, it may be only partial and localized, affecting especially the papillary muscles. In both cases where I have had the opportunity of examining the heart, the fatty degeneration was general and far advanced. There can be no doubt in referring this lesion to the effect of the primary blood change. The valves of the heart are healthy. There are perhaps a few small spots of atheroma of the aorta, but there is no organic change to explain the fatty degeneration of the heart, which must be a part of the general malnutrition, as most clearly pointed out by Ponfick, in his memoir on the "Anæmic form of Fatty Degeneration of the Heart," already referred to. This is further confirmed by the experiments of Perl, which show that anæmia, caused by repeated large losses of blood, induces fatty degeneration of the heart.

The whole organ is flabby and relaxed, so that it does not retain its shape when thrown on a flat surface. Its size is not specially affected. The cavities, especially the auricles, contain soft dark clots. The lining membrane is in some cases stained by imbibition. Occasionally small ecchymoses are observed under the pericardium, and usually there is a small amount of serous effusion in the pericardial sac. In Case III. this effusion was of the colour of claret and water, and contained a few red globules, though its colour was chiefly derived from the dissolved hæmoglobulin.

In some cases, fatty degeneration of the small vessels in various organs has been found.

The *lungs* are extremely anæmic, pale, and crepitant, excepting at the postero-inferior portions, where there is nearly always marked œdematous congestion. There may be small ecchymoses on the pleural surface, and usually there is a moderate amount of serous effusion ($f\bar{3}iv$ to $f\bar{3}x$), yellowish or more frequently reddish in colour.

The *mucous membrane of the stomach* may present small ecchymotic

patches, but is otherwise normal. Ponfick has observed fatty degeneration of the epithelium of the secreting glands. The intestines more frequently present lesions, especially in those cases in which there has previously been diarrhœa, when there is found marked enlargement of the solitary follicles of the small intestines, with or without thinning and softening of the mucous membrane. Even in such cases, the mesenteric glands appear to be but slightly, if at all, enlarged. In cases where no diarrhœa has been present, the intestines are healthy, excepting extreme anæmia of their walls.

The *liver* is not enlarged; its tissue is highly anæmic, and usually presents fatty degeneration. This may either affect the glandular cells uniformly throughout the organ, when the entire surface of a section is not only anæmic and pale, but decidedly yellowish; or, as in Cases II. and III., it may appear chiefly in irregular patches; or finally, as described by Gusserow, it may be observed as minute pale yellowish specks in the tissue. As would naturally be expected, where a lesion is of a purely secondary character and is determined by the general anæmia, its degree varies greatly in different cases.

The *spleen* is almost always slightly enlarged. In the descriptions of this disease will be found the statement repeatedly that enlargement of the spleen is not present. In reality, however, although there is no characteristic lesion, such as leukæmic changes or enlargement of the Malpighian corpuscles, there is in nearly every instance a slight but positive degree of enlargement of the spleen, which in different cases varies from $\frac{1}{4}$ to $\frac{1}{2}$ the original size. In addition to this the pulp has evidently undergone greater change than the other solid organs: it is softened and changed in colour, being purplish or dark brownish-red. It somewhat resembles the swelling of the spleen which follows section of the splenic nerves. And certainly, in an affection such as the one we are discussing, the smallest changes in any of the tissues undoubtedly connected with the elaboration of the blood are highly important.

The *kidneys* frequently present fatty degeneration of their epithelium. This was detected in marked degree in both my own examinations, associated in Case III. with obstruction of many tubules with fatty epithelial cells or granular matter. The capsules of the glands are healthy; the tissue intensely anæmic; there is no increase in connective tissue found; and everything points here, as elsewhere, to the entire dependence of the fatty degeneration upon the primary alteration of the blood.

The *supra-renal capsules* present no special lesion. There is no affection whatever of the *lymphatic glands*.

The peritoneal cavity frequently contains a small quantity of effusion, which may be so great as to attract attention during life.

I am not aware that the *marrow of the bones* has been carefully examined in any case of this peculiar form of anæmia, until the very thorough

study which was made by Prof. Tyson and myself of the specimens from Case III. In one case, graphically described by Ponfick,¹ which seems to have been of this nature, the general character of the marrow is described as "pale, clear grayish-red, quite soft, and of uniform appearance;" but no allusion is made to any more minute examination. I will not waste space by repeating the results given in connection with the case (p. 332), but will merely recall the fact that there existed extreme hyperplasia of the marrow, with production of lymphoid cells, constituting a change similar to that described by Neumann, Ponfick, Mosler, and others, as found in some cases of leukæmia. It is needless to say that it would be premature to advance any theory upon the conditions found in a single case, but if it be shown that in "idiopathic" or "progressive pernicious anæmia" the lesion of the medulla be a constant one, it will establish the truth of the view I now hold, that it is merely the simple medullary form of pseudo-leukæmia.

Diagnosis. Relations to Pseudo-leukæmia.—The recent authors who have described this form of anæmia, assert that it is to be distinguished from pseudo-leukæmia by the absence of enlargement of the glands or of the spleen; but it seems to me more rational first to briefly consider the points of resemblance between the two affections, and then to note the diagnostic symptoms, if any, that may exist. It is not necessary to do more than allude to the following features which both possess in common:—

The insidious and apparently causeless development of languor, debility, and pallor of the surface.

The tendency to palpitation of the heart, to attacks of dyspnœa, to giddiness, tinnitus, and later to dangerous and even fatal syncope.

The failure of appetite, sense of pressure at the epigastrium, and liability to nausea or vomiting on exertion or from indigestion.

The tendency to œdema and passive internal effusions.

The existence of strong anæmic murmurs over the heart and great vessels.

The occurrence of hemorrhages, as petechiæ under the skin or in the retinæ; or from the nose, gums, etc.

The occasional occurrence of albuminuria.

The progressive reduction of the mass of the blood, and especially of the proportion of red globules.

The occurrence of irregular febrile action in many cases.

The absence of emaciation in any marked degree.

The steady progress of debility; the occurrence of wandering delirium, or increâsing coma, and finally death, despite all modes of treatment.

The frequent existence of fatty degeneration of the heart, kidneys, and liver, without other organic disease.

If to these important symptoms there be superadded progressive enlarge-

¹ Ueber Fettherz, p. 10.

ment either of the lymphatic glands or of the spleen, or of both, I think it will be admitted that we have presented the full clinical picture of pseudo-leukæmia. In such cases there may be some additional symptoms depending upon the special organ affected. Thus in cases marked by great enlargement of the glands, we may have pressure upon the trachea, causing dyspnoea and aphonia; upon the intra-thoracic vessels, causing large hydrothorax; upon the nerves of the lumbar or sacral plexus, causing paroxysmal radiating pains; or upon the great vessels of the abdomen, leading to unusually great œdema of the limbs or ascites. So, too, in cases where the spleen is especially implicated, special symptoms, such as ascites, hemorrhage from the stomach or bowels, may be prominent. But it would seem clear that such accidental symptoms cannot affect the fundamental and essential similarity between what I believe to be merely different forms of pseudo-leukæmia, as shown above.

If this be true then, and we have an affection characterized by a profound alteration in *hæmatosis* or the blood-producing function, depending upon lesions in the spleen, lymphatic glands, or marrow of the bones, and leading to the changes in the blood and the peculiar general symptoms we have dwelt upon, it is but right that it should be recognized as a special disease, and receive a name descriptive of its real character. The name of pseudo-leukæmia must certainly be abandoned as unmeaning and confusing. The word cachexia is not sufficiently definite, even when joined with the term "splenic," "lymphatic," or "medullary," according to the tissue chiefly affected. I would, therefore, suggest that, as the essential feature of this whole class of affections is the *defective elaboration of blood*, the term *Anæmatosis* (α , privative, and *αἷματος*, formation of blood) be adopted as a generic name, as distinguished from anæmia, where, without lesions of the blood-making tissues, the mass of the blood or its solid ingredients are diminished.

Relations to Leukæmia or Leucocythæmia.—It is impossible at present to enter upon a discussion of the clinical symptoms presented by leukæmia, and I must limit myself to the assertion, which can be supported, that the only symptom by which cases of the so-called pseudo-leukæmia can be distinguished from the corresponding forms of leukæmia is the increased proportion of white corpuscles found in the blood in the latter affection. In every other respect, as already recognized by Wood, Immermann, and others, their symptoms are indistinguishable. It is clear, also, that in leukæmia the characteristic symptoms and the fatal results are not dependent upon the excess of white corpuscles, but rather upon the profound impairment of the vital properties of the blood and the diminution in the red globules which coexist. Indeed, while these latter changes are constant and progressive, the increase in the white corpuscles appears at irregular and variable periods in the development of the disease, and varies immensely in its degree in different cases. At present it is impossible to decide upon the

exact lesion which determines this increase. We now know that hyperplasia of the marrow, of the spleen, or of the lymphatic glands, even with the development of lymphoid tissue in the liver, may occur and induce profound anæmatisis, but without any leukæmia. It would seem, then, that the changes in the splenic pulp and in the marrow are probably connected with the increased destruction of the red globules. But our knowledge of physiology is not yet sufficiently accurate to enable us to determine why, in certain cases, there is also an increase in the number of white corpuscles: whether there is, in such instances, an increased formation of them connected with hyperplasia of the Malpighian bodies of the spleen, or whether there is some peculiarity in the properties of the white corpuscles in those cases which prevents their conversion into red globules, and thus causes them to accumulate. It is not desirable to speculate about this point, which will probably be soon settled; but the very important conclusion is that a condition so inconstant and irregular, as the increase in the proportion of white corpuscles, should not be made a ground of distinction between groups of cases identical in all other respects. It would certainly be more reasonable to regard all such cases as forming one great class, and to accept such conditions as increase in the white corpuscles as indicating some peculiarity in certain individual cases of the class. Thus, instead of adopting leukæmia as the type, and speaking of pseudo-leukæmia, I would propose to group all of these cases, distinguished by progressive deterioration of the blood connected with lesion of some part of the blood-making apparatus, under the name above suggested of *anæmatisis*, and, if it be deemed necessary, to distinguish those cases which present increase of white corpuscles in addition to the other symptoms by the prefix "*leucocytic*."

Albuminuria.—There is no doubt that some cases of albuminuria bear a close resemblance to the form of anæmatisis we have been considering. But when the small and inconstant amount of albumen in the latter affection is remembered, as well as the absence of tube-casts, the presence of anæmic murmurs without any hypertrophy of the heart, and the more intense degree of the blood alteration, it will not be difficult to avoid the error of confounding them.

Addison's Disease.—This rare form of anæmia, with bronzing of the skin, which Addison first pointed out as connected with a peculiar form of disease (chronic serofulous inflammation) of the supra-renal capsules, can scarcely be distinguished from the other forms of anæmatisis until distinct bronzing of the surface makes its appearance. In fact it is difficult to avoid the conviction that there is more than a mere superficial resemblance between the two affections, and that an analogous disturbance of hæmatisis (possibly connected with lesion of the marrow of the bones) is the essential feature in Addison's disease.

Prognosis.—Unfortunately there is but little to be said upon this point, since in every case where the specific characters of the disease have been

well established, the symptoms have steadily progressed to a fatal result. In the cases of the purely medullary form—where neither spleen nor lymphatic glands are enlarged—it is manifestly difficult to fix the moment when the case is recognized as differing from ordinary severe anæmia. When, however, such an anæmia has appeared causelessly, and progresses despite the use of full doses of iron, suitable food, and favourable hygienic influences, with the peculiar group of general symptoms, and especially with those indicative of fatty degeneration of the heart, there is grave reason for fearing that we have to do with an organic anæmatosis, and that death will result.

Treatment.—From what has been already said, it will be understood that treatment offers little ground for hope in this affection.

In the early stages, rest and change of residence should be recommended. Bearing in mind that not rarely fatty degeneration of the liver and glands of the stomach is present, and that consequently digestion is much impaired, the nutrition should be most carefully attended to, and food administered in the most digestible forms.

Owing to the failure of the appetite and the muscular debility, there would seem to be an indication for the use of tonics, such as vegetable bitters or the mineral acids. But there is no evidence to show that they are productive even of temporary—certainly not of permanent benefit. The same must be said of quinia, which is apt to fail to arrest the irregular febrile movement or to modify the progress of the case, even if the condition of the stomach will permit its continued use in full doses. Notwithstanding this, however, I should certainly recommend the persistent use of quinia for its general tonic action, associated with digitalis, on account of the feebleness of the heart.

Iron would naturally suggest itself as the most appropriate remedy in view of the intense and progressive anæmia. It is found, however, that in some cases it is not well borne, and that, even when given in large doses, it exercises no curative effect. The entire failure of the preparations of iron must be regarded as one of the marked features of difference between this form of anæmia and chlorosis. It is not difficult to explain their want of action, however, when we reflect that the cause of anæmia here is an organic lesion of some of the tissues concerned in the elaboration or in the disintegration of the corpuscular elements of the blood.

In view of the changes which seem to lie at the bottom of these obscure diseases, it would appear that the same powerful alterative medicines which we employ in other cachectic conditions should be relied upon here, and that cod-liver oil, iodine, and arsenic, or some of their preparations, should form a part of our treatment. In the paper of Mr. Broadbent (*Practitioner*, January, 1875), already referred to, the use of *phosphorus* is recommended, on account of its well-known power of influencing profoundly the processes of hæmatosis and nutrition.

Transfusion.—There is, however, one important remedial measure which would undoubtedly suggest itself to every mind. In view of the great reduction in the mass of the blood, and especially in the proportion of red globules, the performance of transfusion would seem strongly indicated. And accordingly in several of the reported cases we find that this operation was either suggested or actually performed. Attractive and promising, however, as it seems at first sight, there does not appear to be any substantial reason for expecting more than temporary benefit from transfusion in such a condition. If the diminished amount of blood constituted the essence of the disease, recovery might be effected by adding fresh and healthy blood. But, since this is but one symptom of a profound lesion of the blood-making apparatus, I can see no good reason for hoping that the morbid process can be arrested, or its effects counteracted merely by adding a small amount of healthy blood to the mass of altered and partly devitalized fluid in the patients' veins. It must further be remembered that the conditions here present must render it necessary to inject a very small quantity of blood at any one time. The heart is uniformly found in a state of fatty degeneration, there is extreme tendency to syncope, and the amount of circulating fluid is very small. It will be easily understood, therefore, that transfusion, to be safely practised in such conditions, must be very cautiously and slowly performed, and the amount of blood injected must be comparatively small. If these precautions be neglected, reasoning would lead us to expect, and experience has unfortunately confirmed the apprehension, that there may be dangerous or even fatal shock after the operation. In Case III. transfusion was twice performed. After the first operation, when only f3ivss defibrinated blood were slowly injected, very alarming symptoms presented themselves in a few hours, and so violent was the depression as to threaten a fatal result. Following these dangerous symptoms, however, there was a short period of apparent improvement resulting from the effects of the transfusion. It was but short-lived, however, and it will be observed that for forty-eight hours preceding the second transfusion, the patient's condition was not so favourable; debility increased, and for the first time petechiæ made their appearance.

The second operation was performed even more slowly and carefully than the first (the amount introduced being but f3vss), and yet it has been seen that the patient survived the operation only twelve hours—dying with greatly increased temperature, rapid pulse and breathing, and delirium followed by coma. This is not the place to discuss the cause of these terrible symptoms which follow some cases of transfusion. They are very frequently observed when the blood of any other animal than man is used for transfusing. But even in cases where human blood is used, it is unfortunately true that they may still occur. It has seemed to me that there is greater danger of such results when the operation is quickly performed,

the blood being introduced rapidly; when the amount of blood used is large, and especially when there is disease of the heart or lungs. Whether there may not be still further danger in such conditions as the one we are discussing, where the blood-making tissues are diseased, is a question to be answered by future experience. The results obtained by others, in the few cases of "progressive pernicious anæmia," where transfusion has been performed, are no more encouraging than those in my own case. It was performed in three of Gusserow's cases (*loc. cit.*). In one, between five and six fluidounces of defibrinated blood were injected without any immediate difficulty, but the patient died the following day in mild delirium. In another instance, the same quantity was introduced by direct transfusion, but with no better results, as the patient was seized with vomiting and chill, followed by high fever, and death ensued in about forty-eight hours. In one case only did temporary benefit follow the transfusion, by the direct method, of about five fluidounces of blood.

In the interesting case of Dr. Chadwick's already alluded to, the amount of blood transfused was unintentionally large, $f\bar{3}xj$, though, owing to an accident, a small hemorrhage of $f\bar{3}iv$ or v subsequently occurred from the vein opened in the operation; but the symptoms which almost immediately followed the operation were precisely similar to those reported in my own case (see page 328), and resulted fatally on the following day.

It is therefore evident that in this form of cachexia, and in all others where similar conditions of fatty degeneration of the heart and greatly diminished mass of blood are present, the only way in which any benefit can be hoped for from transfusion, is by introducing very small quantities of blood at a time, and repeating the operation as frequently as may seem desirable. I would also suggest that the blood should be injected into one of the smaller superficial arteries, so as to diminish the risk of serious disturbance of the heart.

Although, however, up to the present time the operation has not been followed by encouraging results, and although we cannot hope for any radical or permanent benefit from its use, I am still disposed to recommend its performance, strictly in the manner indicated, for the purpose of prolonging life and enabling a better trial of internal remedies to be made. If, however, any alarming symptoms should follow the first small transfusion, it would be more prudent not to attempt a repetition of the operation.

It may be advisable, in concluding this discussion, to briefly state the conclusions which seem to be indicated.

1. Progressive pernicious anæmia is identical with the idiopathic anæmia of Addison, and is in no sense a new disease.
2. It is in reality the medullary form of so-called pseudo-leukæmia.
3. As the primary and essential lesion in this and the analogous conditions (leukæmia and pseudo-leukæmia) appears to be an affection of the

chief blood-making tissues—spleen, lymphatic glands, marrow of the bones—causing defective elaboration of the blood, it seems proper to select some name that will indicate this fact, as *anæmatisis*.

4. The changes in the blood consist of great reduction in its mass, with extreme diminution in the proportion of red globules, without increase in the white corpuscles. There are probably also changes in the vital properties both of the red and white corpuscles.

5. The other lesions, chiefly fatty degeneration of the heart and other organs, passive effusions and hemorrhages, are secondary, and depend upon the blood changes.

6. The symptoms are explicable, in great part, by the state of the blood and the condition of the heart.

7. The disease, when once fully established, appears to be invariably fatal.

8. The remedies which afford most prospect of relief are cod-liver oil, arsenic, and phosphorus.

9. Transfusion is only capable of doing temporary good.

10. The operation is not free from grave danger, owing to the feebleness of the heart and the small amount of blood in the vessels; and, in order to be safely employed, the amount of blood injected must be very small (f3iij), it must be introduced very slowly, and the operation must be repeated at suitable intervals. It adds to the safety of the operation to inject the blood into a small artery instead of a vein.

ART. II.—*Angina Pectoris*. By HAMILTON OSGOOD, M.D., of Philadelphia.

In looking through the literature of this agonizing disorder, one is struck by the great, indeed confusing, variety of opinions which have been put forth concerning its cause and nature. Its terminology is not less embarrassing. The disease was first described by Heberden in 1768. He gave it the name of "*angina pectoris*." Since his day various authors have affixed to this lesion names which express, to a greater or less degree, the opinion of each writer as to its etiology and pathology.

Thus, we have "*sternalgia*" (Good); "*syncope anginosa*" (Parry); "*stenocardia*" (Brera); "*strernodynia syncopalis*" (Sluis); "*neuralgia cardiaca* and *hyperæsthesia plexus cardiaci*" (Romberg); "*hypercinesis* with *hyperæsthesia*" (Bamberger); Bouillaud terms the affection "*neuralgia* of the phrenic nerve," and finally we find the common German term